REMARKS

Status of the Claims

Claims 12-14 and 25-31 are pending in the present application. Claims 1-11 and 15-24 are canceled. Claims 12, 13, 14, and 31 are amended to cancel any reference to "STAT3" or "phosphorylated STAT3." Claim 30 is redrafted in independent form and to correct minor typographical errors. Claim 30 is further amended to specify that "the level of expression of STAT3, phosphorylated STAT3, Smad1 or phosphorylated Smad1 at the nucleic acid level is measured using primer pairs selected from SEQ ID NOS: 21 and 22, or SEQ ID NOS: 5 and 6." Support for the addition of STAT3 in claim 30 is found throughout the specification as originally filed including, *e.g.*, on page 18, lines 30-31. The claims are amended without prejudice or disclaimer. Applicants reserve the right to claim any canceled subject matter in one or more divisional or continuation applications. Reconsideration is respectfully requested.

Substance of the Interview

Applicants and Applicants' representative thank the Examiner for extending the courtesy of an interview on August 19, 2009. The substance of the interview is essentially as described in the interview summary issued by the Examiner on August 25, 2009.

Issues Under 35 U.S.C. § 103 (a)

Claims 12, 13, 25, 27-29, and 31

Claims 12, 13, 25, 27-29, and 31 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Huang *et al.*, *Biochem. J.*, 1999, 342:231-238, ("Huang") in view of PCT Publication No. WO 00/73791 to Yamanouchi *et al.*, ("Yamanouchi"), *see* Office Action, pages 4-5. The Examiner states that Huang discloses a method of contacting a test agent (AGE) with a biological sample, *i.e.*, NRK-49F cells, and determining the level of STAT3 in the biological sample in comparison to the level of expression in a control sample, *i.e.*, NRK-49F cells, which was not contacted with AGE.

The Examiner admits that Huang does not specifically teach that a decrease in expression indicates that the agent is effective in the prevention and/or treatment of proliferative diseases

causing sclerosis or in inhibiting the increase of cellular matrix. However, the Examiner states that Huang appreciated the link between AGE, STAT3 expression, and diabetic nephropathy, which is a disease causing sclerosis, characterized by extracellular matrix accumulation. According to the Examiner, an ordinary artisan would have been motivated to use the link between increased STAT3 levels and diabetic nephropathy to screen for potential drug candidates that would lower STAT3 levels, and accordingly, treat the disease and inhibit increased cellular matrix. The Examiner further states that such a basic screening method is taught by Yamanouchi. Applicants respectfully traverse.

Although Applicants do not agree that the instant claims are obvious in view of Huang and Yamanouchi, the claims are amended in effort to expedite prosecution.

As amended, independent claims 12 and 13 are directed to methods of identifying agents effective in the prevention and/or treatment of proliferative diseases causing sclerosis (claim 12), or effective in inhibiting the increase of extracellular matrix (claim 13) by contacting a test agent with a biological sample; determining the level of expression of at least one substance selected from the group consisting of Smad1 and phosphorylated Smad1 in the biological sample in comparison to the level of expression of the substance in a control sample, wherein a decrease in expression of Smad1 or phosphorylated Smad1 in comparison to the expression level of the substance in the control sample indicates the agent is effective in the prevention and/or treatment of proliferative diseases causing sclerosis (claim 12), or effective in inhibiting the increase of extracellular matrix (claim 13).

Applicants submit that none of the cited references, either alone or in combination, teach or suggest determining the expression levels of Smad1 or phosphorylated Smad1. The cited documents are limited to a discussion of STAT3. Based upon the foregoing, independent claims 12 and 13 are not obvious over the cited references. Dependent claims 25, 27-29, and 31 also incorporate Smad1 or phosphorylated Smad1 and do not specify or encompass STAT3 or phosphorylated STAT3. Accordingly, the dependent claims are also not obvious over the cited references. Withdrawal of the rejection is respectfully requested.

Claim 14

Claim 14 is also rejected under 35 U.S.C. § 103(a) as allegedly obvious over Huang in view of Yanamouchi and further in view of U.S. Patent No. 5,908,925 to Cohen *et al*, ("Cohen"), *see* Office Action, pages 6-7. The Examiner admits that neither Huang nor Yanamouchi describe a method of screening for agents that inhibit the expression of type IV collagen. However, according to the Examiner, diabetic nephropathy was known to be characterized by increased extracellular matrix comprising collagen IV. Therefore, the Examiner alleges that Cohen constitutes evidence that an agent that prevents/treat diabetic nephropathy would also indirectly inhibit collagen IV production. Applicants respectfully traverse.

Although Applicants do not agree that claim 14 is obvious in view of Huang Yanamouchi, and Cohen, claim 14 is amended in an effort to expedite prosecution.

As amended, independent claim 14 is directed to a method of identifying substances effective in inhibiting the expression of α1 type IV collagen, comprising contacting a test agent with a biological sample; determining the level of expression of at least one substance selected from the group consisting of Smad1 and phosphorylated Smad1 in the biological sample in comparison to the level of expression of the substance in a control sample, wherein a decrease in expression of Smad1 or phosphorylated Smad1 in comparison to the expression level of the substance in the control sample indicates the agent is effective in inhibiting the expression of α1 type IV collagen.

Applicants submit that none of the cited references, either alone or in combination, teach or suggest determining the expression levels of Smad1 or phosphorylated Smad1. Based upon the foregoing, claim 14 is not obvious over the cited references. Withdrawal of the rejection is respectfully requested.

Claim 26

Claim 26 is rejected under 35 U.S.C. § 103(a) as allegedly obvious over Huang in view of Yanamouchi and further in view of Wang, *Diabetes*, 2002, 51:3505-3509 ("Wang").
Applicants respectfully traverse.

Claim 26 incorporates all of the elements of independent claims 12, 13, and 14. Accordingly, claim 26 incorporates Smad1 and phosphorylated Smad1. As noted above, neither

Huang nor Yanamouchi, either alone or in combination, teach or suggest these elements. Wang fails to remedy the deficiencies of Huang and Yanamouchi since Wang also fails to teach or suggest Smad1 or phosphorylated Smad1. Accordingly, claim 26 is not obvious over Huang, Yanamouchi and Wang. Withdrawal of the rejection is respectfully requested.

Allowable Subject Matter

The Examiner indicates that claim 30 is allowable if redrafted in independent form, *see* Office Action, page 8. Claim 30 is redrafted in independent form to include all of the elements of previously pending claims 12, 13, and 14. In addition, claim 30 is amended to specify STAT3 in addition to phosphorylated STAT3. Applicants do not believe that this additional element precludes the allowability of the subject matter of previously pending claim 30 since this element is merely added for consistency with the language of the previously pending independent claims. Further, Applicants understand that the Examiner believes that claim 30 is allowable, at least in part, because of the primers specified in claim 30. Accordingly, Applicants submit that claim 30, as amended to specify STAT3, is also allowable.

CONCLUSION

In view of the above amendment and remarks, Applicants believe that the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact L. Parker, Reg. No. 46,046, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated: AUG 27 2009

Respectfully submitted,

By
Gerald M. Murphy, Jr.
Registration No.: 28,977
BIRCH, STEWART, KOLASCH & BIRCH, LLP
8110 Gatehouse Road
Suite 100 East
P.O. Box 747
Falls Church, Virginia 22040-0747
(703) 205-8000
Attorney for Applicant

GMM/LTP/cjw